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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,621	12/27/2001	Peter C. Meltzer	70207/56,579	9295

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GEORGE W. NEUNER, ESQ.
EDWARD & AMGE;, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER

AULAKH, CHARANJIT

ART UNIT PAPER NUMBER

1625

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/033,621

Applicant(s)

MELTZER ET AL.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date g.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. According to paper filed on Feb. 2, 2004, the applicants have elected group I (X represents N) with traverse in response to restriction requirement for further prosecution.
2. Claims 1-45 are pending in the application.

Response to Arguments

3. Applicant's arguments filed on Feb. 2, 2004 regarding restriction requirement have been fully considered but they are not persuasive. The examiner does not agree with the applicant's arguments that examination of all four groups should not impose undue burden. First of all, variable X is critical for the common core of the instant compounds. Secondly, based on the value of variable X, these compounds are classified in different classes and therefore, does constitute a burdensome search. Thus, restriction requirement as indicated is proper and thereby made final.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 30-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating some specific disease conditions where deficiency of dopamine and/or serotonin is implicated such as depression, does not reasonably provide enablement for treating all neurodegenerative diseases, psychiatric dysfunctions, dopamine dysfunctions, cocaine abuse and clinical dysfunctions. The

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specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands, In re*, 858.F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, predictability or unpredictability and the state of the prior art.

The instant compounds are inhibitors of dopamine uptake and serotonin uptake as shown in tables 2 and 3 in the specification. There is huge variation in inhibiting uptake of both dopamine and serotonin as demonstrated by IC50 values since these values range from 55.1 to more than 150,000 nanomoles for dopamine (see compounds 7a and 7d in table 2). There is no teaching in the specification or prior art that deficiency of dopamine and/or serotonin is implicated in the etiology of every known neurodegenerative, psychiatric, dopamine dysfunctions, cocaine abuse and clinical dysfunctions. There are no working examples to show how the instant compounds having inhibitory activity for dopamine and/or serotonin uptake will have utility for treating all known neurodegenerative, psychiatric, dopamine dysfunctions, cocaine

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abuse and clinical dysfunctions. It is well known in the art that hyperactivity of dopamine system is implicated in the étiology of certain psychiatric disorders such as schizophrenia or psychoses since antipsychotics are the treatment of choice and produce their beneficial effect by blocking dopamine receptors in the limbic system. The instant dopamine uptake inhibitors will actually worsen psychoses or shizophrenia since they will enhance the levels of dopamine in the synapse and therefore, will not have utility for treating psychoses or schizophrenia. Similarly, there is no teaching in the prior art that deficiency of dopamine and /or serotonin is implicated in the etiology of Alzheimer disease, a neurodegenerative disease. In absence of such teachings, guidance and working examples, it would require undue experimentation to demonstrate the effectiveness of the instant compounds in treating all known neurodegenerative, psychiatric, dopamine dysfunctions, cocaine abuse and clinical dysfunctions.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 14, 17, 19-28, 30-33, 35, 36, 38, 39 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "amino group" in claim 12. There is insufficient antecedent basis for this limitation in the claim.

In claim 17, the term ---member of the group --- is vague. The applicants are suggested to use the language ---member selected from the group -----.

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Claim 24 is a substantial duplicate of claim 19.

In claims 19 and 24, compounds ee and ff recite benzoyloxy in the 6 or 7 position.

However, according to claim 1, R2 is either OH or =O. Therefore, there is no antecedent basis for this limitation in claim 1.

In claims 20-23, variable X is defined as N3. There is no antecedent basis for this limitation in claim 1. It should be NR3.

In claims 25-28, the applicants mention inhibiting serotonin or dopamine uptake of monoamine or dopamine transporter. It is the same thing. The applicants should either use the word ---inhibiting serotonin uptake --- or inhibiting serotonin transporter— in claims 25 and 27 and same for dopamine in claims 28 and delete claim 26. Also, it is not clear whether inhibition is achieved in vitro or in vivo? In claims 25 and 26.

In claims 30, 31 and 42, the term ---clinical dysfunction is indefinite since its meaning is not clear and furthermore, is not defined in the specification.

Claims 32 is substantial duplicate of claim 33.

Claim 35 is substantial duplicate of claim 36.

Claim 38 is substantial duplicate of claim 39.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1-29, 41, 44 and 45 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Meltzer (J. Med. Chem. Vol. 44, 2001, cited on applicants form 1449). Meltzer discloses synthesis of 6- and 7-hydroxy-8-azabicyclo[3.2.1]octanes and their binding affinity for the dopamine and serotonin transporters. The compounds disclosed

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in schemes 1-6 (see compounds 7a-d, 8a-d, 14, 15, 17, 18, 19, 20, 23, 26), figures 1 - 2 and tables 2-3 by Meltzer clearly anticipate the instant claims.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-9, 12, 14-16, 18, 20, 22, 25-29, 41, 44 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao (J. Med. Chem., cited on applicants form 1449).

Zhao discloses chemical synthesis and pharmacology of 6- and 7-hydroxylated 2-carbomethoxy-3-(p-tolyl)tropanes. The compounds disclosed in schemes 2-5 and table 1 anticipate the instant claims when R2 represents OH in the instant compounds of claim 1.

10. Claims 1-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Meltzer (WO 99/02526, cited on applicants form 1449).

Meltzer discloses tropane analogs and methods for inhibition of monoamine transport. The compounds of formulae I where m is 0, II and III (see pages 7-8), compounds 11, 20 and 21 (see figures 1 and 2) and table III (pages 55-60, specially first compound on page 56) disclosed by Meltzer anticipate the instant claims when R2 represents OH in the instant compounds of claim 1.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Meltzer (U.S. 6,353,105).

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The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Meltzer discloses tropane analogs and methods for inhibition of monoamine transport.

The compounds of formulae I where m is 0, II and III (see col. 5, line 10 to col. 6, line 18), compounds 11, 20 and 21 (see figures 1 and 2) as well as claims 1-11 and 21-35 disclosed by Meltzer anticipate the instant claims when R₂ represents OH in the instant compounds of claim 1.

12. Claims 1-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Meltzer (U.S. 6,670,375).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Meltzer discloses tropane analogs and methods for inhibition of monoamine transport.

The compounds of formulae I where m is 0, II and III (see col. 5, line 5 to col. 6, line 6), compounds 10, 11, 20 and 21 (see figures 1 and 2) as well as claims 1-23 disclosed by

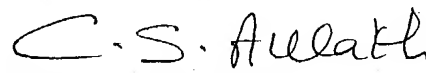
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Meltzer anticipate the instant claims when R2 represents OH in the instant compounds of claim1.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on (703)308-4698. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Charanjit S. Aulakh
Primary Examiner
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